

Finding Meaning in Complexity

"The process is more complex than was previously appreciated," could be the final sentence of a great many research articles. Discoveries continually uncover important nuances in well-studied cellular processes and unveil entirely new swaths of biology ripe for study. As scientists, our appreciation of the complexity in pathways, cells, tissues, and organisms is today being driven in many fields by ever-expanding ways to measure, model, and analyze. Increasingly, the challenge is to find meaning in all of this complexity.

In this vein, Ronald Evans and David Mangelsdorf (Review, page 255) offer a perspective on nuclear hormone receptors, highlighting how the discovery of an apparently straightforward dimerization interaction between retinoid X receptors unlocked the complex realm of receptor-based signaling, with its many implications for eukaryotic physiology and therapeutic interventions. In an Essay, Robert Weinberg (page 267) shares his scientific journey, moving from discovery to discovery, aiming to decipher the intricacies of both why and how cancer cells become tumorigenic. Although hallmarks or harbingers of a simple logic behind each step in tumorigenesis have emerged, complexity rears its head in understanding how cellular heterogeneity and layered crosstalk with the microenvironment influence pathophysiology. This era of sequencing, genomics, and systems biology have clearly added additional layers of information and complexity to a disease that is already thought to be extremely complex. Reflecting further on the common theme of complexity in biology, we asked five Nobel Laureates to use their crystal balls to forecast emerging themes (Voices, page 272). Paul Nurse advocates for the need to comprehend core functional elements to make sense of biological systems, while Joseph Goldstein and Michael Brown introduce the importance of thresholds in biology. Carol Greider explains how size takes precedence over function in telomere biology, and finally, David Baltimore predicts that harnessing the complex powers of the immune system in the form of gene therapy will pave the way for efficacious cancer treatments.

